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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,721	09/05/2003	Xiaowu Pang	NIH202.001C1	8676

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EXAMINER	
MOSHER, MARY	
ART UNIT	**PAPER NUMBER**
1648	

NOTIFICATION DATE	DELIVERY MODE
09/17/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/656,721	PANG ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) 1,3-7,9-15 and 21-24 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2, 8, 16-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648, examiner Mosher.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/9/2007 has been entered.

Election/Restrictions

Claims 1, 3-7, 9-15, 21-24 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/17/2006.

Response to Arguments

Claims 2, 8, 17-20 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Westaway et al. (US 6893866), in view of Schlesinger et al. (Journal of General Virology 68:853-857, 1987), Bartenschlager (US 6630343), and Fields et al (Virology Third edition, p. 931-937, 1966).

Claim 16 was previously rejected under 35 U.S.C. 103(a) as being unpatentable over Westaway et al., Schlesinger et al., Bartenschlager, and Fields et al. as applied to claims 2, 8, 17-20 above, and further in view of Khromykh et al (Journal of Virology 71:1497-1505, 1997).

In response to the above rejections, applicant argues the prosecution history leading to the Westaway patent: because the disclosure was held to be not enabling for the entire genus Flavivirus, the patent does not teach a genus, and therefore cannot make obvious the species Dengue. Therefore applicant argues that the teachings of Westaway are limited to the species Kunjin. Applicant further argues that the phylogenetic and sequence divergence between Kunjin, hepatitis C, BVDV, and Dengue made it impossible to predict dengue replicons. Applicant further argues that Schlesinger did not provide motivation to substitute a Dengue replicon for the Kunjin replicon since Schlesinger dealt with the NS1 subunit, and that following the Westaway teachings for inserting heterologous genes into the 3' untranslated region would not have worked with Dengue.

Many of these arguments are unconvincing, for the following reasons. In regard to the Westaway patent, while a reference must enable someone to practice the invention in order to anticipate under §102(b), a non-enabling reference may qualify as prior art for the purpose of determining obviousness under §103a (e.g. *Symbol Technologies Inc. v. Opticon Inc.* 19 USPQ2d 1241, at 1247). It is noted that Westaway did not provide descriptive support for any subgroup or species of flavivirus other than Kunjin, so the Patent Office prosecution would not have addressed the issue of whether

or not Westaway's disclosure (alone or combined with the ordinary knowledge of those skilled in the art) was enabling for some additional species of flaviviruses, such as better-known species like Dengue. Even if not enabling for replicons of all 70 species of the genus Flavivirus, Westaway explicitly suggests applying the patent teachings to flaviviruses other than Kunjin, and this suggestion is not meaningless to those in the art. Also, the genus/species guidelines provided in MPEP 2144.08 refer to the analysis used for a single-reference 103 rejection, which is not the situation in either the previous or the current rejections. In regard to phylogenetic and sequence diversity, the prior successful development of subgenomic replicons in the JEV group of the flavivirus genus of family Flaviviridae, and the hepacivirus and pestivirus genera of the family Flaviviridae indicates that phylogenetic and sequence diversity do not present any insurmountable barrier to those skilled in the art. In regard to the location of heterologous genes in Westaway, the patent does not teach only insertion in the 3' UTR, the patent also teaches preferred insertion in the structural gene region, see column 3 lines 18-22.

In regard to Schlesinger, the reference makes the point that dengue is a flavivirus of interest. However, the examiner agrees with applicant that the disclosure in Schlesinger does not particularly suggest a Dengue replicon. Therefore, the rejections of record are withdrawn in favor of the new rejections below.

Claim Rejections - 35 USC § 103

Claims 2, 8, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over [Westaway (US6893866) and/or Khromykh et al (Journal of Virology 71:1497-

1505, 1997; in IDS) and/or Khromykh (Current Opinion in Molecular Therapeutics 2(5):555-569, 2000; in IDS)] in view of Polo et al (Journal of Virology 71:5366-5374, 1997; in IDS). As discussed above and in previous Office actions, Westaway teaches a flavivirus subgenomic replicon for Kunjin virus, and explicitly suggests replicons "derived from any flavivirus RNA." Khromykh 1997 refers to previous work describing the preparation of a stable full-length cDNA copy of Kunjin RNA capable of producing an infectious RNA transcript in vitro, and describes extending the work by preparing a self-replicating RNA (subgenomic replicon) with a deletion in the region of the genome encoding structural components of the virion. See the first paragraph on page 1497. Khromykh 2000 teaches that subgenomic replicon vectors were known in the art for a wide variety of positive stranded RNA viruses, including alphaviruses, picornaviruses, pestiviruses, hepaciviruses, and two species of flaviviruses (Kunjin and Yellow Fever). All of the replicons had deletion of some or all of the structural genes (which could be provided in trans for packaging) while retaining nonstructural genes and cis-acting RNA elements required for amplification.

These primary references differ from the claims in that none of them teach a Dengue type 2 subgenomic replicon. However, Polo teaches that Dengue is a flavivirus of interest. Polo further teaches a stable, full-length cDNA copy of Dengue type 2 RNA capable of producing an infectious RNA transcript in vitro. It would have been within the ordinary skill of the art to modify the infectious RNA system of Polo to create a subgenomic replicon by gene deletion, as taught for the analogous Kunjin virus by the primary references, for the purpose of obtaining another useful flaviviral expression

vector and for the purpose of studying dengue RNA replication. A reasonable expectation of success is indicated by the prior knowledge (in Polo) of how to generate infectious self-replicating full-genome Dengue RNA, and the demonstrated success of others (especially in Khromykh 2000) in converting a variety of different full-genome infectious RNAs into subgenomic replicons by methods of structural gene deletion. Therefore the invention as a whole is prima facie obvious, absent unexpected results.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Khromykh et al (Journal of Virology 71:1497-1505, 1997) in view of Polo et al (Journal of Virology 71:5366-5374, 1997) and Fields (1996), optionally in view of [Westaway (US6893866) and/or Khromykh (Current Opinion in Molecular Therapeutics 2(5):555-569, 2000; in IDS)]. Claim 16 differs from the above claims in requiring the replicon to retain at least the first nucleotide of the C coding sequence and the last nucleotide of the E coding sequence. Khromykh 1997 specifically teaches retaining some or all of the C sequence, particularly a RNA cyclization sequence, in the Kunjin replicon. Khromykh 1997 also teaches retaining the end of the E sequence to retain a signal sequence for NS1 processing. Fields teaches that these two cis-acting regions are characteristic of flaviviruses in general. Therefore, one skilled in the art would have been motivated to retain these sequences in a Dengue replicon, for the same reasons that Khromykh 1977 retained the sequences in the Kunjin replicon. The invention as a whole is prima facie obvious, absent unexpected results.

Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over [Westaway (US6893866) and/or Khromykh (Current Opinion in Molecular Therapeutics

2(5):555-569, 2000; in IDS)] in view of Polo et al (Journal of Virology 71:5366-5374, 1997), optionally in view of Khromykh et al (Journal of Virology 71:1497-1505, 1997). These claims differ from the above in requiring a body-treating composition comprising the subgenomic replicon, or in requiring the replicon packaged in a virus-like particle. Both Westaway and Khromykh 2000 teach packaging of replicons by providing structural proteins in trans, and both teach the use of the packaged replicons for inducing immune responses in vivo. Therefore, one skilled in the art would have been motivated to package Dengue replicons in a similar manner, for similar use in vivo. The invention as a whole is prima facie obvious, absent unexpected results.

Double Patenting

Claims 2, 8, 16, 17-20 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/194,342, for reasons of record.

Claims 2, 8, 16, 17-20 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8, 22-27 of copending Application No. 11/192,923, for reasons of record.

Since these are not the only rejections remaining in the earliest-filed application, the provisional rejections are not withdrawn.

Conclusion

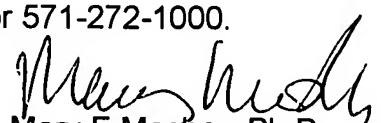
No claims are allowed.

Kovacs et al (US7034141) is cited as of interest, in presenting patented claims reciting dengue replicons, see claim 8 for example.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on varying dates and times; please leave a message..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mary E Mosher, Ph.D.
Primary Examiner
Art Unit 1648

9/6/07